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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,487	07/19/2006	Peter Francis Joseph O'Hare	BJS-620-421	9941

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EXAMINER	
KINSEY, NICOLE	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,487	O'HARE ET AL.	
	Examiner	Art Unit	
	Nicole E. Kinsey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/3/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 11 and 12 are objected to because of the following informalities: Claim 11 recites " . . .an aggregated composition according to claim 1 in to deliver . . . ." This does not make sense. Claim 12 does not end with a period. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9-11 provide for the use of an aggregated composition, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 9-11 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). "Use" claims are non-statutory under 35 U.S.C. 101. Therefore, claims 9-11 have been withdrawn from consideration as being drawn to non-statutory subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claim is drawn to sub-fragments that are modified by deletion or substitution.

The written description rejection is made because the claims are interpreted as being drawn to a genus of modified products. The applicable standard for the written description requirement can be found in MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Probe Inc., 63 USPQ2d 1609; Vas- Cath Inc. v. Mahurkar, 19 USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CAFC 2004). To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present is a statement in the specification that "e.g. the cysteine of

the 191-220 peptide can be replaced by an alanine." There is no disclosure of any particular amino acid(s) that can be deleted or other amino acids that can be substituted or where the deletions or substitutions can occur. There is no indication of the structure or length of the sub-fragments that are to be modified by deletion or substitution. Further, there is no recited function of the modified sub-fragments, nor any guidance relating to how the modifications either affect or do not affect the function of the sub-fragments.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

The court clearly states in Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented what is claimed. As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of modified VP22 sub-fragments. Given that the specification has only described one modification (i.e., the cysteine of the 191-220 peptide replaced by alanine), the full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph.

Claims 1-8 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for VP22 from HSV-1 or HSV-2, does not reasonably provide enablement for VP22 from other sources such as VZV, BHV-1, EHV-1 or MDV. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

Nature of the invention. The claims are drawn to an aggregated composition comprising (a) a sub-fragment of the 159-301 fragment of full length VP22 protein, and (b) an oligonucleotide or polynucleotide.

Breadth of the claims. The claims are very broad, encompassing a composition comprising a sub-fragment of the 159-301 fragment of any VP22.

Working examples. There is one working example showing sub-fragments from HSV-2 VP22. There are no working examples showing the effectiveness of sub-fragments from other sources of VP22 such as VZV, BHV-1, EHV-1 or MDV.

Guidance in the specification. The specification provides no guidance regarding compositions comprising sub-fragments from other sources of VP22 such as VZV, GHV-1, EHV-1 or MDV.

Predictability of the art. The amino acid residue numbering of 159-301 is specific for HSV VP22. Using amino acid residues 159-301 from VZV, BHV, or MDV would not yield the same functional 159-301 fragment that one would obtain from HSV. Therefore, one of ordinary skill in the art could not use the amino acid numbering (i.e.,

residues 159-301) provided for HSV VP22 to obtain the same fragment with the same function from VZV, BHV-1 or MDV.

Given the breadth of the claims, the lack of working examples, the lack of guidance in the specification, and the predictability of the art, it would require undue experimentation for one skilled in the art to use the claimed composition and method.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 8 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 8 and 12, the phrase "for example" (e.g.) renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 7-8 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Hare et al. (WO 00/53722).

The claims are drawn to an aggregated composition comprising a sub-fragment of the 159-301 fragment of full length VP22 protein and an oligonucleotide or polynucleotide.

O'Hare et al. discloses an aggregated composition comprising a sub-fragment of the 159-301 fragment of full length VP22 protein and an oligonucleotide or polynucleotide (see Example 6, page 15, lines 1-14) and a method of making the composition (see page 11, lines 8-12). O'Hare et al. further discloses that the compositions can contain a pharmaceutically acceptable carrier (see page 9, lines 13-21). The VP22 can be labeled with a tag (see page 3, lines 9-15) and be part of a fusion protein (see page 5, lines 12-28). O'Hare et al. discloses compositions to deliver substances to cells (see page 4, line 24 to page 5, line 6). The compositions of O'Hare et al. can also contain a photosensitizing molecule to act as a disaggregating agent (see page 10, lines 11-28).

Claims 1, 2, 4, 7-8 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by O'Hare et al. (U.S. Patent Application No. 2004/0171044).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome

either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

O'Hare et al. discloses an aggregated composition comprising a sub-fragment of the 159-301 fragment of full length VP22 protein and an oligonucleotide or polynucleotide (see Example 6) and a method of making the composition (see Example 1). O'Hare et al. further discloses that the compositions can contain a pharmaceutically acceptable carrier (see paragraph [0044]). The VP22 can be labeled with a tag (see paragraph [0012]) and be part of a fusion protein (see paragraphs [0023] to [0025]). O'Hare et al. discloses compositions to deliver substances to cells (see paragraphs [0041] to [0041]). The compositions of O'Hare et al. can also contain a photosensitizing molecule to act as a disaggregating agent (see paragraphs [0049] to [0050]).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Hare et al. (WO 00/53722) as evidenced by Normand et al. (Journal of Biological Chemistry, 2001, 276(18):15042-15050).

The claims are drawn to an aggregated composition where the sub-fragments are amino acid residues 194-226, 191-220 or 191-226 of VP22, wherein the sub-fragment 194-226 is labeled with KRRRR or K at the C-terminal end or wherein the sub-fragments are modified by deletion or substitution.

The teachings of O'Hare et al. are outlined above. O'Hare et al. does not teach the specific sub-fragments, labeling the sub-fragments or modifying the sub-fragments.

According to section 2144.05 of the MPEP, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine

where in a disclosed set of percentage ranges is the optimum combination of percentages.")

A particular parameter must first be recognized as a result-effective variable, i.e., a variable, which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In the instant application, it was well known in the art that region 159-301 of HSV VP22 forms aggregates and retains the transport functionality of full length VP22 (see O'Hare et al. page 3,lines 2-9 and see Normand et al.). Therefore, determining other regions within the 159-301 fragment that also contain these properties by, for example, creating N-terminal or C-terminal truncations or creating deletion or substitution mutants, is routine experimentation. Further, O'Hare et al. teaches that the fragments can be labeled with, for example, tags at the C-terminus or N-terminus for purification, detection, etc. (see O'Hare et al. page 3,lines 9-15). Therefore, it would have been obvious for one of ordinary skill in the art to substitute any of the tags, labels, or sequences known in the art for the C-terminus or N-terminus tags/labels taught by O'Hare et al. for a particular purpose (i.e., purification, detection, translocation, nuclear localization, etc.), and the results of the substitution would have been predictable. For example, fusing a nuclear localization signal to a peptide will result in the peptide localizing to the nucleus in a cell. Accordingly, the instant invention is obvious over O'Hare et al.

Claims 3, 5, and 6 are rejected under 35 U.S.C. 103(a) as being obvious over O'Hare et al. (U.S. Patent Application No. 2004/0171044) as evidenced by Normand et al. (Journal of Biological Chemistry, 2001, 276(18):15042-15050).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claims are drawn to an aggregated composition where the sub-fragments are amino acid residues 194-226, 191-220 or 191-226 of VP22, wherein the sub-fragment 194-226 is labeled with KRRRR or K at the C-terminal end or wherein the sub-fragments are modified by deletion or substitution.

The teachings of O'Hare et al. are outlined above. O'Hare et al. does not teach the specific sub-fragments, labeling the sub-fragments or modifying the sub-fragments.

According to section 2144.05 of the MPEP, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.")

A particular parameter must first be recognized as a result-effective variable, i.e., a variable, which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In the instant application, it was well known in the art that region 159-301 of HSV VP22 form aggregates and retains the transport functionality of full length VP22 (see paragraph [0012] and see Normand et al.). Therefore, determining other regions within the 159-301 fragment that also contain these properties by, for example, creating N-terminal or C-terminal truncations or creating deletion or substitution mutants, is routine experimentation. Further, O'Hare et al. teaches that the fragments can be labeled with, for example, tags

at the C-terminus or N-terminus for purification, detection, etc. (see paragraph [0012]). Therefore, it would have been obvious for one of ordinary skill in the art to substitute any of the tags, labels, or sequences known in the art for the C-terminus or N-terminus tags/labels taught by O'Hare et al. for a particular purpose (i.e., purification, detection, translocation, nuclear localization, etc.), and the results of the substitution would have been predictable. For example, fusing a nuclear localization signal to a peptide will result in the peptide localizing to the nucleus in a cell. Accordingly, the instant invention is obvious over O'Hare et al.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole E. Kinsey, Ph.D. whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nicole E. Kinsey, Ph.D.
Examiner
Art Unit 1648

/nk/

/Stacy B. Chen/ 8-10-2007
Primary Examiner, TC1600